IN THE UNITED STATES DISTRICT COURT FOR THE MIDDLE DISTRICT OF TENNESSEE NASHVILLE DIVISION

RUTH SMITH, Individually and as Widow for the Use and Benefit of Herself and the Next of Kin of RICHARD SMITH, Deceased,	)	**Case #: 3:05-00444**
	)	**Judge Trauger**
Plaintiff,	)	
-against-	)	
PFIZER INC., PARKE-DAVIS, a division of Warner-Lambert Company and Warner-Lambert Company LLC, WARNER-LAMBERT COMPANY, WARNER-LAMBERT COMPANY LLC and JOHN DOE(S) 1-10,	)	
Defendants.	)	

MEMORANDUM IN SUPPORT OF PLAINTIFF'S MOTION *IN LIMINE* TO PRECLUDE ANY MENTION AT TRIAL BY DEFENDANTS THAT THE THE NEURONTIN PACKAGE INSERT WAS LABELED TO WARN AGAINST COMPLETED SUICIDE PRIOR TO THE DECEMBER 21, 2005 LABELING CHANGE

Plaintiff Ruth Smith, as the Widow for the use and benefit of herself and the next of kin of Richard Smith, deceased, by and through her undersigned counsel, respectfully requests an order precluding Defendants Pfizer Inc. and Warner-Lambert Company LLC from providing any comment, evidence, testimony, inference or document that the Neurontin package insert was labeled to warn against completed suicide prior to the December 21, 2005 labeling change.

INTRODUCTION

On December 21, 2005, long after the death of Richard Smith, Defendants changed the Neurontin package insert to include suicide within the label. Before then Defendants considered suicide to be an unlabeled event. After that point, Defendants considered suicide to be a labeled event. Evidence offered that suicide was a labeled event before December 2005 is contrary to

communications between the company and the Food and Drug Administration and communications exchanged internally within the company during their normal course of business. This evidence also is contrary to the actions of the company in the routine course of their business. Furthermore, the statements by the company constitute admissions that are not hearsay under Fed. R. Evid. 801(d)(2).

Accordingly, Defendants should not be permitted to tell the jury that suicide was labeled when during the course of its business suicide was unlabeled except for the purposes of defending itself in litigation Any such testimony would be patently false and would serve only to confuse the jury and must be excluded under Fed. R. Evid. 403.

PROCEDURAL HISTORY OF THE DECEMBER 21, 2005 LABELING CHANGE

On October 20, 2005, the FDA contacted Defendants by e-mail and requested that they change the Neurontin label with respect to suicide-related events:

> Regarding NDA 20-235, 20-882, 21-129, 21-216, 21-397, and 21-424, the following are our latest suggestions for labeling changes pertaining to suicide-related events.
>
> 1. In the "Other Adverse Events Observed During All Clinical Trials: Clinical Trials in Adults and Adolescents with Epilepsy" section, delete "suicidal" and "suicide gesture" and add "suicide attempt" as an infrequent event and "suicide" as a rare event.

See Declaration of Kenneth B. Fromson, Ex. A.

Following this e-mail on October 27, 2005, the FDA sent another e-mail in response to a phone call from Defendants' employee Manini Patel. In the e-mail the FDA stated the following:

> Regarding your phone call, below are our answers:
>
> 1. We think that "suicidal" should be deleted because its meaning is unclear. It is not clear what, as an adjective, it is referring to since there is no noun following it.

> 2. "Suicide gesture" is a less clear term than "suicide attempt." If interpreted as meaning "suicide attempt," the current placement of the term with respect to the frequency of its occurrence in clinical trials is incorrect. According to the analysis submitted in September, 2004, suicide attempts occurred in .12% of patients participating in nonplacebo-controlled adult add-on epilepsy trials and 0.17% of patients in adult add-on placebo-controlled studies. Therefore, "suicide attempt" should be listed as an infrequent adverse event.
>
> 3. Because suicides occurred in 0.02% of patients participating in non-placebo-controlled adult add-on epilepsy trials, suicide should be listed as a rare adverse event in this section (describing events that occurred in adult add-on epilepsy trials).

Fromson Decl., Ex. B.

> On November 18, 2005, Defendants contacted the FDA and wrote the following:
>
> I am responding to your email dated October 20, 2005 regarding the FDA's suggested labeling changes for Neurontin and your email dated October 27, 2005 providing additional clarifications.
>
> Pfizer has reviewed FDA's suggested revisions as well as the additional clarifications and will be making the changes requested by the FDA. Pfizer would also like to respond to two of the clarifications provided by the Agency in the October 27 email regarding the event terms “suicidal” and “suicide gesture”.

Fromson Decl., Ex. C.

The FDA replied to Defendants on November 27, 2005, telling Defendants to make the change. Fromson Decl., Ex. D (Plaintiff’s Ex. 4). On December 21, 2005, Defendants submitted a formal request to change the label. Fromson Decl., Ex. E. In the change request, the company stated that:

> As agreed, the USPI has been revised with the following changes:
>
> - “Suicide attempt” will replace the terms “suicidal” and “suicide gesture,” and will be listed as an infrequent event under the “Other Adverse Events Observed During All Clinical Trials: Clinical Trials in Adults and Adolescents with Epilepsy” section.
>
> - “Suicide” will be ***added*** as a rare event in this same section.

- "Suicide attempt" will be listed as an infrequent event in the "Clinical Trials in Adults With Neuropathic Pain of Various Etiologies" section of the revised label.

Finally, on May 3, 2006, the FDA approved the labeling change. Fromson Decl., Ex. F.

From the above correspondence, it is clear that the FDA was asking the company to add suicide to the label. At no point did Defendants protest that suicide was to be added to the label. The company's own correspondence stated that it was going to add suicide to the label. Therefore, the only reasonable conclusion is that suicide was added to the label on December 21, 2005.

PRIOR TO DECEMBER 21, 2005 DEFENDANTS' INTERNAL DOCUMENTS AND ACTIONS DEMONSTRATE THAT SUICIDE WAS UNLABELED FOR NEURONTIN

Defendants Exhibit 7049(196) is the periodic report for Neurontin in the period August 19, 2004 through August 18, 2005. Fromson Decl., Ex. G. This document is the annual report that the company provides to the FDA in accordance with 21 C.F.R. § 314.80(c). On page 8 of this document, the company provides a line listing for the number of serious unlabeled, serious labeled, and non-serious reports for each adverse event term. *Id.* at 8. Starting on page 22 and moving to page 23, the company lists psychiatric terms which include events related to suicidality – completed suicide, suicide attempt, and suicidal ideation. *Id.* at 22, 23. For completed suicide, the company list 71 events and all 71 are serious unlabeled. *Id.* Therefore, as of at least the time of this report, the company considered completed suicide to be unlabeled.

There is a clear contrast between the 2004 periodic report for Neurontin and the 2005 report covering the period from August 19, 2005 through August 18, 2006. Fromson Decl., Ex. H. The 2005 report reflects that the company added completed suicide to the label as discussed above. *Id.* On page 5 of the 2005 report is a MedWatch form for suicide. *Id.* at 5. The report was considered by the company to be a periodic report. According to 21 C.F.R. § 314.80, a

report that is not both serious ***and*** unlabeled is submitted as a periodic report. Since suicide involves death, all reports of completed suicide are serious by definition. *See* 21 C.F.R. § 314.80(a). Therefore, the report must be labeled to qualify as a periodic report. Page 18 of the 2005 report confirms the labeled status of the event. *Id.* at 18. At the top of the page, the heading is for Serious Labeled events. *Id.* The third report on the page is the completed suicide report from page 5 of the report, despite the erroneous page reference within the report. *Id.* at 5. This is confirmed by comparing the Manufacturer's report number.

As with the 2004 report, there is a tabular table for each event providing the number of serious unlabeled, serious labeled, and non-serious events. Fromson Decl., Ex. G. On page 43 of the 2005 report, the company has a listing for completed suicide and reflects that there were 52 serious unlabeled events and 38 serious labeled events. Fromson Decl., Ex. H. This is consistent with the labeling change after May 3, 2006.

Finally, page 49 of the 2005 report reflects changes made to the labeling in the time period:

> The following same changes were made in the package inserts:
> In the **ADVERSE REACTIONS** section, **Other Adverse Events Observed During All Clinical Trials** subsection, under Clinical Trials in Adults and Adolescents (Except Clinical Trials in Neuropathic Pain), the following changes were made:
>
> The number of patients was changed from 2074 to 4717.
>
> In the Nervous System paragraph, the events of "suicidal" and "suicidal gesture" were deleted, and replaced with the events of "suicide attempt" and "suicide".
> In the **ADVERSE REACTIONS** section, **Clinical Trials in Adults with Neuropathic Pain of Various Etiologies** subsection, in the Nervous System paragraph, **the event of "suicide attempt" was added.**

Fromson Decl., Ex. H.

These changes are consistent with the labeling change submitted by the company on December 21, 2005 (Fromson Decl., Ex. E), and approved by the FDA on May 3, 2006 Fromson Decl., Ex. F.

Plaintiff also reviewed the periodic reports for August 19, 2003, through August 18, 2004 (Defs. Exhibit 7049(192)), and August 19, 2002 through August 18, 2003 (Defs. Exhibit 7049(171)). For these two reports there were 16 and 21 reports, respectively, of completed suicide and all of the events were serious and unlabeled.

Aside from the periodic reports, Plaintiff also reviewed the ArisG adverse event database produced by Defendants and listed as Plaintiff Trial Exhibit 5311. The database contains data through February 23, 2005, and was produced to Plaintiff shortly after that time. Plaintiff has prepared a chart listing the completed suicide reports within the database and the labeled status for each report. Fromson Decl., Ex. I. As can be seen for every report, the company database shows that the suicide event was unlisted within the United States label through the entire duration of the database.

Therefore, it is indisputable that in the eyes of the company and through its actions that suicide was not labeled before the December 21, 2005 labeling change.

DEFENDANTS WILL LIKELY CLAIM THAT
THE NEURONTIN LABEL DID WARN FOR SUICIDE

Defendants may argue that the label did warn for suicide because the term suicidal includes the term suicide. This is incorrect and is contrary to the applicable regulations. First, according to 21 C.F.R § 314.80(a):

> *Unexpected adverse drug experience.*
> Any adverse drug experience that is not listed in the current labeling for the drug product. This includes events that may be symptomatically and pathophysiologically related to an event listed in the labeling, but differ from the event because of greater severity or specificity. For example,

> under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the labeling only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the labeling only listed cerebral vascular accidents.

Fromson Decl., Ex. J.

Further, according to the testimony of Defendants' expert Janet Arrowsmith-Lowe, completed suicide is more specific than the term suicidal because not everyone who is "suicidal" actually commits suicide.

> Does everybody who exhibits suicidal behavior commit suicide?
>
> MR. BARNES:
> Objection, asked and answered. She's answered it three times.
>
> BY MR. ALTMAN:
> Q. She has not answered it.
>
> A. What do you mean by suicide?
>
> Q. Commits -- do you know what the term to commit suicide means?
>
> A. Do you -- what do you mean by suicide? Do you mean that someone has actually killed themselves?
>
> Q. That's what to commit suicide means.
>
> A. No, it doesn't.
>
> Q. That's fine.
>
> A. I don't think so. I think you were asking me if they -- if suicide -- about suicidal behavior. That's not the same as actually a completed suicide.
>
> Q. Okay. That's what I'm saying. So everybody -- so not everybody who -- who exhibits suicidal behavior actually completes suicide, correct?
>
> A. Yes, I believe I've -- I've said that several times, yes.

Fromson Decl., Ex. K at 136:14-137:10.

Moreover, completed suicide that implies a death is obviously more serious than any term that means something less than death. As noted above in the correspondence from the FDA, the company never intended that the terms suicidal or suicide gesture included completed suicides:

> The term ”suicidal” has been included in the Neurontin US Package Insert since the original approval of the add-on Epilepsy indication in 1993. The term “suicidal” was taken from the modified CoStart dictionary and included the following reported investigator terms – “attempted suicide” and “suicide ideation.” The labeled term “suicidal,” therefore, included the term “suicide attempt” and was an infrequent event listed in the “Other Adverse Events Observed During All Clinical Trials: Clinical Trials in Adults and Adolescents with Epilepsy” section.
>
> The event term “suicide gesture” was not intended to encompass “suicide attempt,” but instead reflects self- injurious behavior associated with no intent to die. In other words, “suicide gesture” describes behavior that is intended to effect change in others or the environment or intended to relieve distress (e.g., superficial cuts or scratches, hitting/banging, or burns), and was a rare event listed in the “Other Adverse Events Observed During All Clinical Trials: Clinical Trials in Adults and Adolescents with Epilepsy” section. Nonetheless, Pfizer will agree to make the change at the FDA's request.

Fromson Decl., Ex. C.

The absolute fallacy in Defendants’ argument is demonstrated by the fact that if suicide was in fact in the label prior to December 21, 2005, why did the FDA ask the company to add suicide to the label and why did the company agree to the FDA request? The plain answer is suicide was not labeled and it is only because of litigation that Defendants now claim that suicide was in the label all along.

CONCLUSION

Therefore, Plaintiff respectfully requests that the Court grant this motion and order that Defendants be prohibited from introducing evidence or testimony that in any way suggests that prior to the December 21, 2005 labeling change, which was approved in May, 2006, the company label for their drug Neurontin included a warning for completed suicide.

Dated: April 16, 2010

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on this the 16th day of April, 2010, I electronically filed the foregoing document with the Clerk of the Court, United States District Court for the Middle District of Tennessee, using the CM/ECF system. True and correct copies of the foregoing documents are being served via the Court's CM/ECF system on the following:

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